Amendm nts to th Claims

Please amend Claims 54 and 64 as shown below. Please cancel Claim 83. This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1. (Previously Cancelled) An antibody which catalyzes hydrolysis of β- amyloid at a predetermined amide linkage.

2. (Previously Cancelled) The antibody of Claim 1 which catalyzes hydrolysis of the amide linkage between residues 39 and 40 of β- amyloid.

3. (Previously Cancelled) The antibody of Claim 1 which catalyzes hydrolysis of the amide linkage between residues 40 and 41 of β- amyloid.

4. (Previously Cancelled) The antibody of Claim 1 which catalyzes hydrolysis of the amide linkage between residues 41 and 42 of β- amyloid.

5. (Previously Cancelled) The antibody of Claim 1 which preferentially binds a transition state analog which mimics the transition state adopted by β- amyloid during hydrolysis at a predetermined amide linkage, and also binds to natural β- amyloid with sufficient affinity to detect using an ELISA.

6. (Previously Cancelled) The antibody of Claim 1 which preferentially binds a transition state analog which mimics the transition state adopted by β- amyloid during hydrolysis at a predetermined amide linkage, and does not bind natural β- amyloid with sufficient affinity to detect using an ELISA.

7. (Previously Cancelled) A vectorized antibody which is characterized by the ability to cross the blood brain barrier and the ability to catalyze the hydrolysis of β- amyloid at a predetermined amide linkage.

8. (Previously Cancelled) The vectorized antibody of Claim 7 which is a bispecific antibody.

9. (Previously Cancelled) The vectorized antibody of Claim 8 which has a first specificity for the transferrin receptor and a second specificity for a transition state adopted by β-amyloid during hydrolysis.

10. (Previously Cancelled) The vectorized antibody of Claim 9 which catalyzes hydrolysis of β- amyloid between residues 39 and 40.

11. (Previously Cancelled) A method for sequestering free β- amyloid in the bloodstream of an animal, comprising the steps:
    a) providing antibodies specific for β- amyloid; and
    b) intravenously administering the antibodies to the animal in an amount sufficient to increase retention of β- amyloid in the circulation.

12. (Previously Cancelled) A method for sequestering free β- amyloid in the bloodstream of an animal, comprising the steps:
    a) providing an antigen comprised of an epitope which is present on endogenous β-amyloid; and
    b) immunizing the animal with the antigen of step a) under conditions appropriate for the generation of antibodies which bind endogenous β- amyloid.

13. (Previously Cancelled) A method for reducing levels of β- amyloid in the brain of an animal, comprising the steps:
    a) providing antibodies specific for β- amyloid endogenous to the animal; and
    b) intravenously administering the antibodies to the animal in an amount sufficient to increase retention of β- amyloid in the circulation of the animal.

14. (Previously Cancelled) The method of Claim 13 wherein the antibodies specific for β-amyloid are catalytic antibodies which catalyze hydrolysis of β-amyloid at a predetermined amide linkage.

15. (Previously Cancelled) The method of Claim 13 wherein the antibodies are monoclonal.

16. (Previously Cancelled) The method of Claim 13 wherein the antibodies are polyclonal.

17. (Previously Cancelled) The method of Claim 13 wherein the antibodies specifically recognize epitopes on the C-terminus of β-amyloid$_{1-43}$.

18. (Previously Cancelled) A method for reducing levels of β-amyloid in the brain of an animal, comprising the steps:
    a) providing an antigen comprised of an epitope which is present on β-amyloid endogenous to the animal; and
    b) immunizing the animal with the antigen of step a) under conditions appropriate for the generation of antibodies which bind endogenous β-amyloid.

19. (Previously Cancelled) The method of Claim 18 wherein the antigen is a transition state analog which mimics the transition state adopted by β-amyloid during hydrolysis at a predetermined amide linkage.

20. (Previously Cancelled) The method of Claim 18 wherein the antigen is comprised of $A\beta_{10-25}$.

21. (Previously Cancelled) The method of Claim 19 wherein the antibodies generated have a higher affinity for the transition state analog than for natural β-amyloid.

22. (Previously Cancelled) The method of Claim 19 wherein the antibodies generated catalyze hydrolysis of endogenous β-amyloid.

23. (Previously Cancelled) A method for preventing the formation of amyloid plaques in the brain of an animal, comprising the steps:
    a) providing an antigen comprised of an epitope which is present on ÿ- amyloid endogenous to the animal; and
    b) immunizing the animal with the antigen of step a) under conditions appropriate for the generation of antibodies which bind endogenous β-amyloid.

24. (Previously Cancelled) The method of Claim 23 wherein the antigen is a transition state analog which mimics the transition state adopted by β-amyloid during hydrolysis at a predetermined amide linkage.

25. (Previously Cancelled) A method for reducing levels of circulating β-amyloid in an animal, comprising the steps:
    a) providing an antigen comprised of an epitope which is a mimic of a predetermined hydrolysis transition state of a β-amyloid polypeptide endogenous to the animal; and
    b) immunizing the animal with the antigen of step a) under conditions appropriate for the generation of antibodies to the β-amyloid hydrolysis transition state.

26. (Previously Cancelled) A method for reducing levels of circulating β-amyloid in an animal, comprising the steps:
    a) providing antibodies which catalyze the hydrolysis of β-amyloid endogenous to the animal; and
    b) intravenously administering the antibodies to the animal.

27. (Previously Cancelled) A method for preventing the formation of amyloid plaques in the brain of an animal, comprising the steps:
    a) providing antibodies which catalyze hydrolysis of β-amyloid produced by the animal at a predetermined amide linkage; and
    b) administering the antibodies to the animal in an amount sufficient to cause a significant reduction in β-amyloid levels in the blood of the animal.

28. (Previously Cancelled) A method for reducing levels of β-amyloid in the brain of an animal, comprising the steps:
    a) providing vectorized bispecific antibodies competent to transcytose across the blood brain barrier, which catalyze hydrolysis of β-amyloid of the animal at a predetermined amide linkage; and
    b) intravenously administering the antibodies to the animal.

29. (Previously Cancelled) The method of Claim 28 wherein the vectorized bispecific antibodies specifically bind the transferrin receptor.

30. (Previously Cancelled) The method of Claim 28 wherein the vectorized bispecific antibodies catalyze hydrolysis of the amide linkage between residues 39 and 40 of β-amyloid.

31. (Previously Cancelled) A method for disaggregating amyloid plaques present in the brain of an animal comprising the steps:

a) providing vectorized bispecific antibodies competent to transcytose across the blood brain barrier, which catalyze hydrolysis of β-amyloid produced by the animal at a predetermined amide linkage; and

b) intravenously administering the antibodies to the animal in an amount sufficient to cause significant reduction in β-amyloid levels in the brain of the animal.

32. (Previously Cancelled) A method for disaggregating amyloid plaques present in the brain of an animal, comprising the steps:

a) providing antibodies which catalyze hydrolysis of β-amyloid produced by the animal at a predetermined amide linkage; and

b) administering the antibodies to the animal.

33. (Previously Cancelled) A method for generating antibodies which catalyze hydrolysis of a protein or polypeptide comprising the steps:

a) providing an antigen, the antigen being comprised of an epitope which has a statine analog which mimics the conformation of a predetermined hydrolysis transition state of the polypeptide;

b) immunizing an animal with the antigen under conditions appropriate for the generation of antibodies to the hydrolysis transition state.

34. (Previously Cancelled) The method of Claim 33 wherein the protein is β-amyloid.

35. (Previously Cancelled) A method for generating antibodies which catalyze hydrolysis of a protein or polypeptide comprising the steps:

a) providing an antigen, the antigen being comprised of an epitope which has a reduced peptide bond analog which mimics the conformation of a predetermined hydrolysis transition state of the polypeptide;

b) immunizing an animal with the antigen under conditions appropriate for the generation of antibodies to the hydrolysis transition state.

36. (Previously Cancelled) The method of Claim 35 wherein the protein is β-amyloid.

37. (Previously Added) A method for inhibiting the formation of β-amyloid plaques in the brain of a human, the method comprising:

a) providing a β-amyloid epitope; and

b) administering the epitope of step a) to the human under conditions appropriate for the stimulation of an immune response directed toward the epitope, the immune response being characterized by the generation of circulating antibodies which bind specifically to the epitope present on endogenous β-amyloid in the human.

38. (Previously Added) The method of Claim 37 wherein the epitope of step a) is administered in an adjuvant formulation.

39. (Previously Added) The method of Claim 38 wherein the adjuvant formulation comprises an alum adsorption.

40. (Previously Added) The method of Claim 38 wherein the adjuvant formulation comprises oil emulsion.

41. (Previously Added) The method of Claim 37 wherein the binding of circulating antibodies to endogenous β-amyloid detectably alters the equilibrium distribution of free β-amyloid in circulation versus free β-amyloid in the brain of the human.

42. (Previously Added) The method of Claim 37 wherein the epitope of β-amyloid is linked to an immunogenic carrier moiety.

43. (Previously Added) The method of Claim 42 wherein the immunogenic carrier moiety is diphtheria toxoid.

44. (Previously Added) The method of Claim 42 wherein the immunogenic carrier moiety is hepatitis B core antigen.

45. (Previously Added) The method of Claim 37 wherein the epitope is provided as β-amyloid peptide $A\beta_{1-43}$.

46. (Previously Added) The method of Claim 37 wherein the epitope is provided as β-amyloid peptide $A\beta_{1-42}$.

47. (Previously Added) The method of Claim 37 wherein the epitope is provided as β-amyloid peptide $A\beta_{1-41}$.

48. (Previously Added) The method of Claim 37 wherein the epitope is provided as β-amyloid peptide $A\beta_{1-40}$.

49. (Previously Added) The method of Claim 37 wherein the epitope is provided as a peptide fragment of β-amyloid, the peptide fragment being derived from the N-terminal region of the β-amyloid peptide $A\beta_{1-43}$.

50. (Previously Added) The method of Claim 37 wherein the epitope is provided as a peptide fragment of β-amyloid, the peptide fragment being derived from the central region of the β-amyloid peptide $A\beta_{1-43}$.

51. (Previously Added) The method of Claim 37 wherein the epitope is provided as a peptide fragment of β-amyloid, the peptide fragment being derived from the C-terminal region of β-amyloid peptide.

52. (Previously Added) The method of Claim 37 which results in the stimulation of an immune response which includes the production of antibodies which bind specifically to immobilized β-amyloid peptides in an *in vitro* binding assay, the immobilized β-amyloid peptides being selected from the group consisting of: $A\beta_{1-16}$, $A\beta_{14-25}$, $A\beta_{34-43}$, $A\beta_{1-40}$ and $A\beta_{1-43}$.

53. (Previously Added) The method of Claim 37 which results in the stimulation of an immune response which includes the production of antibodies which bind specifically to β-amyloid in solution.

54. (Currently Amended) A method for inhibiting the formation of β-amyloid aggregates and plaques in the brain of a human, the method comprising:

a) providing a plurality of peptide fragments derived from β-amyloid peptide $A\beta_{1-43}$, each peptide fragment comprising one or more β-amyloid epitopes; and

b) administering the plurality of peptide fragments of step a) to the human under conditions appropriate for the stimulation of an immune response directed toward the β-amyloid epitopes, the immune response being characterized by the generation of circulating antibodies which bind specifically to one or more epitopes present on endogenous β-amyloid in the human.

55. (Previously Added) The method of Claim 54 which results in the stimulation of an immune response which includes the production of antibodies which bind specifically to immobilized β-amyloid peptides in an *in vitro* binding assay, the immobilized β-amyloid peptides being selected from the group consisting of: $A\beta_{1-16}$, $A\beta_{14-25}$, $A\beta_{34-43}$, $A\beta_{1-40}$ and $A\beta_{1-43}$.

56. (Previously Added) The method of Claim 54 which results in the stimulation of an immune response which includes the production of antibodies which bind specifically to β-amyloid in solution.

57. (Previously Added) The method of Claim 54 wherein at least one epitope is provided as a peptide fragment of β-amyloid, the peptide fragment being derived from the N-terminal region of the β-amyloid peptide $A\beta_{1-43}$.

58. (Previously Added) The method of Claim 54 wherein at least one epitope is provided as a peptide fragment of β-amyloid, the peptide fragment being derived from the central region of the β-amyloid peptide $A\beta_{1-43}$.

59. (Previously Added) The method of Claim 54 wherein at least one epitope is provided as a peptide fragment of β-amyloid, the peptide fragment being derived from the C-terminal region of β-amyloid peptide.

60. (Previously Added) A method for inhibiting the formation of β-amyloid plaques in the brain of a human, the method comprising:

a) providing an antibody which binds specifically to an epitope of β-amyloid peptide; and

b) delivering the antibody of step a) into the circulation of the human at concentrations sufficient to detectably alter the equilibrium distribution of free β-amyloid peptide in circulation versus free β-amyloid peptide in the brain of the human.

61. (Previously Added) The method of Claim 60 wherein the antibody has the ability to inhibit the formation of β-amyloid plaques.

62. (Previously Added) The method Claim 60 wherein the antibody has the ability to disaggregate preformed β-amyloid plaques.

63. (Previously Added) The method of Claim 60 wherein the antibody has the ability to hydrolytically cleave β-amyloid.

64. (Currently Amended) A vaccine composition comprising a β–amyloid epitope in ~~an~~ a human compatible adjuvant formulation.

65. (Previously Added) The vaccine composition of Claim 64 wherein the β-amyloid epitope is linked to an immunogenic carrier moiety.

66. (Previously Added) The vaccine composition of Claim 65 wherein the immunogenic carrier moiety is diphtheria toxoid.

67. (Previously Added) The vaccine composition of Claim 65 wherein the immunogenic carrier moiety is hepatitis B core antigen.

68. (Previously Added) The vaccine composition of Claim 64 wherein the epitope is provided as β-amyloid peptide $A\beta_{1-43}$.

69. (Previously Added) The vaccine composition of Claim 64 wherein the epitope is provided as β-amyloid peptide $A\beta_{1-42}$.

70. (Previously Added) The vaccine composition of Claim 64 wherein the epitope is provided as β-amyloid peptide $A\beta_{1-41}$.

71. (Previously Added) The vaccine composition of Claim 64 wherein the epitope is provided as β-amyloid peptide $A\beta_{1-40}$.

72. (Previously Added) The vaccine composition of Claim 64 wherein the epitope is provided as a peptide fragment of β-amyloid, the peptide fragment being derived from the N-terminal region of the β-amyloid peptide $A\beta_{1-43}$.

73. (Previously Added) The vaccine composition of Claim 64 wherein the epitope is provided as a peptide fragment of β-amyloid, the peptide fragment being derived from the central region of the β-amyloid peptide $A\beta_{1-43}$.

74. (Previously Added) The vaccine composition of Claim 64 wherein the epitope is provided as a peptide fragment of β-amyloid, the peptide fragment being derived from the C-terminal region of the β-amyloid peptide $A\beta_{1-43}$.

75. (Previously Added) The vaccine composition of Claim 64 which results in the stimulation of an immune response which includes the production of antibodies which bind specifically to immobilized β-amyloid peptides in an *in vitro* binding assay, the immobilized β-amyloid peptides being selected from the group consisting of: $A\beta_{1-16}$, $A\beta_{14-25}$, $A\beta_{34-43}$, $A\beta_{1-40}$ and $A\beta_{1-43}$.

76. (Previously Added) The vaccine composition of Claim 64 which results in the stimulation of an immune response which includes the production of antibodies which bind specifically to β-amyloid.

77. (Previously Added) The vaccine composition of Claim 64 wherein the β-amyloid is free in solution.

78. (Previously Added) The vaccine composition of Claim 64 wherein the β-amyloid is aggregated.

79. (Previously Added) A method for inhibiting the formation of β-amyloid plaques in the brain of a human, the method comprising:

a) providing an antibody which binds specifically to an epitope of β-amyloid peptide; and

b) delivering the antibody of step a) by direct infusion into the brain of the human.

80. (Previously Added) The method of Claim 79 wherein the antibody has the ability to inhibit the formation of β-amyloid plaques.

81. (Previously Added) The method of Claim 79 wherein the antibody has the ability to disaggregate preformed β-amyloid plaques.

82. (Previously Added) The method of Claim 79 wherein the antibody has the ability to hydrolytically cleave β-amyloid.

83. (Currently Cancelled) A method for inhibiting the formation of beta-amyloid plaques in the brain of a human, the method comprising:

a) providing an antigen comprised of an epitope which is a mimic of a predetermined hydrolysis transition state of a beta-amyloid polypeptide endogenous to the animal; and

b) immunizing the animal with the antigen of step a) under conditions appropriate for the generation of antibodies to the beta-amyloid transition state.

84. (Previously Added) A method for inhibiting the formation of beta-amyloid plaques in the brain of a human, the method comprising:

a) providing an antibody which catalyzes the hydrolysis beta-amyloid; and

b) administering the antibody to the human in an amount sufficient to increase retention of beta-amyloid in the circulation.